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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EWOLDT, GERALD R	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,686	ORBAN, TIHAMER	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,7-10,13,14,16-19,21-25,27,28 and 30-34* is/are pending in the application.

4a) Of the above claim(s) *1,4,5,7-9,25,27,28,30,31 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10, 13, 14, 16-19, 21-24, 32, 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and remarks, filed 8/04/05, are acknowledged. In view of Applicant's amendment the previous rejection under the second paragraph of 35 U.S.C. 112 has been withdrawn.

2. Note Applicant's election without traverse of Group II, Claims 10-24, and the autoantigen species: insulin B-chain, filed 11/22/04. In the instant amendment Applicant has amended all pending claims to read on a pharmaceutical composition comprising human preproinsulin and fragments and variants thereof. Because Applicant has previously elected the insulin B-chain, and an Office action has been issued, said species cannot now be changed. Accordingly, the instant claims are under examination only as they read on an insulin B-chain fragment of human preproinsulin.

3. Claims 1, 4, 5, 7-9, 25, 27, 28, 30, 31, and 34 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 10, 13, 14, 16-19, 21-24, and newly added Claims 32 and 33 are being acted upon.

4. Applicant's new declaration is acknowledged.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

6. Claims 10, 13, 16, 17, and newly added Claim 31, stand/are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ramiya et al. (1996, IDS).

As set forth previously, Ramiya et al. teaches a pharmaceutical composition comprising a type 1 diabetes autoantigen, specifically, a synthetic human insulin B-chain fragment comprising amino acids 33-37 of SEQ ID NO:1 (SHLVE) in the oil-based adjuvant IFA (see particularly page 350, column 1, *Subcutaneous immunizations of NOD mice* and peptide p(1-15)).

Applicant's arguments, filed 8/04/05, have been fully considered but they are not persuasive. Applicant argues that the amending of the claims to recite Montanide ISA as the adjuvant overcomes the rejection.

Applicant is advised that the specification makes clear (see for example, page 6, lines 8-10) that IFA is an equivalent of Montanide ISA.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claim 18 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Ramiya et al. (1996, IDS) in view of U.S. Patent No. 6,462,185.

As set forth previously, Ramiya et al. has bee discussed above.

The reference teaching differs from the claimed invention only in that it does not teach solubilizing the insulin B-chain peptide in urea.

The '185 patent teaches that urea buffers are routinely used to solubilize essentially insoluble proteins (see particularly column 21, lines 61-63).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to solubilize the insulin B-chain peptide of Ramiya et al. in the urea buffer of the '185 patent. One of ordinary skill in the art would have been motivated to employ a urea buffer given the teaching of the '185 patent that urea buffers can be used to solubilize even essentially insoluble proteins.

Applicant's arguments, filed 8/04/05, have been fully considered but they are not persuasive. Applicant argues that as Ramiya et al. is defective, the rejection should be withdrawn.

See the Examiner's response in Section 6 above.

9. Claims 21, 23, 24, and newly added Claim 34 stand/are rejected under 35 U.S.C. 103(a) as being unpatentable over Ramiya et al. (1996, IDS) in view of U.S. Patent No. 4,281,061.

As set forth previously, Ramiya et al. has been discussed above.

The reference teaching differs from the claimed invention only in that it does not teach the peptide of the claims in kit form.

The '061 patent teaches that reagents can be provided in kits as a matter of convenience and for the optimization of their use (see particularly column 22, line 62 - column 23, line 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide the insulin B-chain peptide of Ramiya et al. in the kit form of the '061 patent. One of ordinary skill in the art would have been motivated to provide said kit given the teachings of the '061 patent that reagents can be provided in kits as a matter of convenience and for the optimization of their use. Note that the kit of the '061 patent does not include instructions. MPEP 706.03(a) makes it clear that printed matter, which would include instructions, does not add patentable weight to a product because printed matter does not comprise a statutory class of invention. See also MPEP 2111.03 wherein it states that, while intended use recitations and other types of functional language cannot be entirely disregarded, in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the limitations of the claims. Such is the case with the invention of the instant claims.

Applicant's arguments, filed 8/04/05, have been fully considered but they are not persuasive. Applicant argues that as Ramiya et al. is defective, the rejection should be withdrawn.

See the Examiner's response in Section 6 above.

10. Claim 22 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Ramiya et al. (1996, IDS) in view of U.S. Patent No. 4,281,061, as applied to Claims 21, 23, and 24 above, in further view of U.S. Patent No. 5,447,843.

As set forth previously, Ramiya et al. and the '061 patent have been discussed above.

The combined reference teachings differ from the claimed invention only in that they do not teach a lyophilized insulin B-chain peptide autoantigen.

The '843 patent teaches that proteins in kits can be lyophilized for convenience (see particularly column 10, lines 24-35).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide the insulin B-chain peptide in lyophilized form, as taught by the '843 patent, in the kit of the combined Ramiya et al. and '061 patent references. One of ordinary skill in the art would have been motivated to provide said lyophilized insulin B-chain peptide given the teachings of the '843 patent that proteins in kits can be lyophilized for convenience.

Applicant's arguments, filed 8/04/05, have been fully considered but they are not persuasive. Applicant argues that as Ramiya et al. is defective, the rejection should be withdrawn.

See the Examiner's response in Section 6 above.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 10, 13, 14, 16-19, 21-24, and newly added Claims 32 and 33 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, There is insufficient written description to show that Applicant was in possession of "an immunologically active fragment of a variant" of the autoantigen of the instant claims.

The specification discloses no such fragment or variants. The specification does disclose that variants can include sequence and non-sequence modifications. Non-sequence modifications include acetylations, methylations, phosphorylations, carboxylations, and glycosylations. Sequence modifications include naturally occurring and non-naturally occurring amino acids, as well as substitutions, deletions and insertions, both conservative and non-conservative. It is clear then that the claims encompass an essentially unlimited genus of peptides, none of which are disclosed. While the specification, at pages 32-36, may disclose how to make the claimed fragments and variants, said disclosure is not an actual description of the products made. Accordingly, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genus of peptides. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant's arguments, filed 8/04/05, have been fully considered but they are not persuasive. Applicant reviews the disclosure of the specification and then argues that the claimed genus is limited both functionally and quantitatively. Thus, in view of Example 14 of the Written Description Guidelines, Applicant argues that the written description requirement has been satisfied.

While the claimed genus may be limited functionally, there is nothing more than Applicant's assertion that it is limited

quantitatively. Indeed, the specification discloses that in addition to the unlimited number of sequence modifications that might be encompassed, nonsequence modifications not limited to acetylation, methylation, phosphorylation, carboxylation, and glycosylation are also encompassed by the claimed genus. Clearly, this is not a quantitatively limited genus as is asserted by Applicant. Regarding Example 14 of the Written Description Guidelines, Applicant fails to note that said example encompasses only variants that have function *and* 95% or greater sequence identity to the claimed sequence. Applicant is advised to see Example 13 wherein the variants lacking that critical limitation are found not to satisfy the written description requirement.

13. The following are new grounds for rejection necessitated by Applicant's amendment.

14. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Ramiya et al. (1996, of record) in view of Cox et al. 1997.

Ramiya et al. has bee discussed above.

The reference teaching differs from the claimed invention only in that it does not teach a pharmaceutical composition comprising a Montanide ISA adjuvant.

Cox et al. teaches that Montanide ISA adjuvants are preferred because they have a superior safety profile (see particularly page 250, column 2, last sentence and reference 29).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce the pharmaceutical composition of Ramiya et al. substituting a Montanide ISA adjuvant for the IFA of the reference. One of ordinary skill in the art would have been motivated to make said substitution given the teachings of Cox et al. that Montanide ISA adjuvants comprise a superior safety profile.

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it

> is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 17 and 24 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed, for the reasons of record, specifically, the recitation of "wherein the Montanide ISA comprises Montanide 80". This is a new matter rejection.

Applicant indicates that no new matter has been added, however, the only disclosure in the specification regarding Montanide 80 is at page 13, "Examples of emulsifiers or surfactants include Arlacel A, mannide oleate (e.g., Montanide 80-mannide monooleate), anhydrous mannitol/oleic acid ester: polyoxyethylene or polyoxypropylene". This disclosure does not support the new limitation of the claims.

17. No claim is allowed.

18. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571)272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

20. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact

the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

10/7/05

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